B7 Cont

b) an oleaginous base including olive oil, sunflower oil, almond oil, cod liver oil and castor oil; and

c) a pharmaceutically acceptable excipient.

B2

25. (Amended) A method for treating burns and other injuries and disorders of the skin or mucosal surface, which comprises applying to the site in need of treatment an effective amount of a composition consisting essentially of: a) from about 10 and about 50 percent by weight of beeswax; b) an oleaginous base including olive oil, sunflower oil, almond oil, cod liver oil and castor oil; and c) a pharmaceutically acceptable excipient.

REMARKS

Upon entry of this amendment, claims 1, 2, 4-15, 17, 18, and 22-27 would be pending in the present application, claim 3 having been canceled without prejudice. This amendment also amends claims 1 and 25. A markup of the amendments to these claims is attached hereto as Appendix B. Adequate support for the amendments can be found on page 1, lines 12 and 15; page 3, lines 2-4 and lines 25-29; page 4, lines 9-12 and elsewhere throughout the specification, as filed. Accordingly, it is believed that no new matter has been introduced to the pending application.

I. The Invention

The invention is directed to a novel composition that can be applied topically to the skin or mucosa for the purpose of treating burns and other injuries and disorders. In particular, the claimed invention consists essentially of three essential elements: a recited range by weight percent of beeswax, an oleaginous base having five recited natural oils, and a pharmaceutically acceptable excipient. Remarkably, when applied to a burn, lesion or other injury or disorder, the claimed composition provides relief from pain and provides a soothing layer that promotes healing despite the absence of an "active" or "therapeutic" ingredient, which one of ordinary skill in the art would typically associate with a standard treatment of burns or similar injuries. As discussed further below, in comparative studies with a standard burn treatment

containing a sulfa drug, the claimed invention performs in an unexpectedly superior fashion under a number of objective and subjective criteria.

II. The Rejections Under Section 103(a)

The pending claims, save for claim 23, stand rejected as allegedly being unpatentable under 35 U.S.C. 103(a) over the disclosure of U.S. Patent No. 5,503,825 (the "'825 patent"). The Examiner points out that the '825 patent is directed to topical compositions that have healing properties. Moreover, the Examiner states that the "composition may comprise, *as a vehicle*, a mixture of any of mineral oil (liquid petroleum jelly excipient), vegetable oils such as castor oil, almond oil, olive oil and sunflower oil, animal oils such as cod liver oil, waxes such as beeswax and fatty acids, *inter alia* (col. 4, lines 18-53)." (first emphasis added) See, bottom of page 2 of the Office Action. At page 3 of the Office Action, the Examiner adds that "[a]ll of the instantly claimed components are well known and commonly used in the art. It is within the skill in the art to combine well-known and commonly used components expecting to obtain an art useful composition," and at page 4, remarks further that "[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to prepare the composition of US '825 using any desired combination of ingredients with the reasonable expectation of obtaining a topical composition with improved healing properties."

All the pending claims, save for claim 23, stand rejected also as being allegedly unpatentable over a combination of the disclosures of the '825 patent and U.S. Patent No. 4,386,067 (the "'067 patent"). Claim 23 stands rejected as allegedly being unpatentable over a combination of the '825 patent and the '067 patent, and, in addition, in view of U.S. Patent No. 5,597,849 (the "'849 patent").

These rejections under Section 103(a) are respectfully traversed for the following reasons.

The claimed invention is directed to a novel composition that can be applied topically to the skin or mucosa for the purpose of treating burns and other injuries and disorders. What is surprising and unexpected about the claimed invention is that while the claimed invention possesses no "active" or "therapeutic" agent, which one of ordinary skill in the pharmaceutical arts would consider the equivalent of a steroid

or sulfa drug commonly associated with standard burn treatments, it provides superior results in the treatment of burns when compared with silver sulfadiazine, a drug preparation that is a standard for treatment of burns.

Indeed, the Examiner herself recognizes that the disclosure of the principal reference, as any person of ordinary skill in the pharmaceutical arts would, refers to the claimed components as among a long laundry list of substances considered to be a "vehicle," which "may be any cosmetic vehicle which, in the case that aloe vera is used, does not react with aloe vera, and is otherwise toxicologically and pharmaceutically acceptable." Col. 4, lines 18-21, of the '825 patent. These substances being considered cosmetic vehicles are, thus, by all reasonable expectations incapable of exhibiting any therapeutic effects. Consistent with this proposition, the Summary of the Invention section of the '825 patent states in pertinent part that:

> The lip balm is preferably one which contains aloe as an active ingredient. In this case, the aloe and the salt are considered to be the main active ingredients, and any cosmetic vehicle which does not adversely [a]ffect the efficacy and stability can be used as the vehicle for these active ingredients.

Col. 2, lines 47-52, of the '825 patent. Only an unreasonable reading of the teachings of the '825 patent would lead one to attach any potential therapeutic benefits to a collection of cosmetic "vehicles," as enumerated in the '825 patent. Certainly at the time the present invention was made, the inventor of the methods claimed in the '825 patent attached no therapeutic significance to "vehicle," failing to recite the identity of even one vehicle in claim 1, which states only:

> A method of restoring chapped or burned lips, comprising topically administering to such lips a mixture comprising: up to 35 wt% aloe vera gel; from 3 wt% or more salt; and a pharmaceutically acceptable medium.

As described in the Tabuke Declaration, attached hereto as Appendix A, not only were there surprising therapeutic benefits associated with the claimed invention, but the claimed invention provided unexpectedly superior results over a standard treatment for burns, silver sulfadiazine. Hence, Applicant respectfully asserts that even assuming *arguendo* that the claimed components could have been properly

selected from the long laundry list of "vehicles" provided in the '825 patent, one of ordinary skill in the art would have had no expectation, let alone any reasonable expectation, of success that the claimed invention would have provided any therapeutic benefits to a subject suffering from burns and other injuries and disorders of the skin or mucosal surface.

In addition, the Examiner cites the '067 patent for the proposition that "oils [are] commonly used in topical cosmetic applications." The Examiner concludes that it would have been obvious "to prepare the composition of US '825 using any combination of commonly used oils as disclosed in US '067 with the reasonable expectation of obtaining a topical composition with improved healing properties." Page 4 of the Office Action. The Applicant respectfully disagrees to the extent that the Examiner believes that she has established the notion that one of ordinary skill would have had any expectation that a cosmetic composition would exhibit healing properties. As explained above, a mere "vehicle" carries with it no reasonable expectation of therapeutic benefits.

In the '825 patent, the active ingredients were aloe vera and salt. In the '067 patent, the active ingredient(s) are the non-saponifiable portions of certain oils – that is, certain extracts from oils, which include:

> . . . at least thirty different components some of which have a chemical composition that heretofore have remained undetermined.
>
> It has been possible to characterize squalene, beta-carotene and carotenoids, aromatic compounds, C_{16} to C_{32} hydrocarbons for the majority of unsaturated compounds, vegetable sterols (beta-sitosterol, stigmasterol, campesterol, brassicasterol and other unknown sterols) or animal sterols, terpenes and free terpene alcohols (beta-amyrine, butyrospermol, cyclo-artenol), C_{12} to C_{20} aliphatic alcohols and tocopherols.
>
> Non-glyceride substances of vegetable oils have also been found . . .

See, e.g., col. 1, lines 46-58, of the '067 patent. In U.S. Patent No. 5,597,849 (the "'849 patent," which is cited by the Examiner for the alleged obviousness of butylhydroxytoluene or BHT as a preservative), the active ingredients can be anything other than the waxes and oils of the "vehicle." For example in the Abstract, the subject matter of the '849 patent is described as:

> Stick formulations for topical delivery of water soluble and/or water insoluble agents are disclosed. The stick formulations may contain steroids, antibiotics, antifungals, antihistamines anti inflammatories or local anesthetics. The *vehicles comprise a combination of waxes and oils* and a surfactant in embodiments involving water soluble agents. Methods for preparing the various stick formulations are also disclosed. (emphasis added)

Hence, contrary to the Examiner's contention, it should be abundantly clear that the state of the art calls for an "active" ingredient, other than the types of substances recited in the claimed invention, to be present in compositions reasonable expected to have any therapeutic or healing properties. Yet, while missing such an "active" ingredient, the claimed invention still outperforms a standard treatment for burns. See, Tabuke Declaration, Appendix A. According to the MPEP, the omission of an element with retention of the element's function is an indicia of non-obviousness. MPEP §2144.04, Part II, B.

Moreover, Applicant respectfully asserts that there is nothing in the references of record, which would point one of ordinary skill to select the claimed components. The Examiner has provided no reasoning or evidence that one of ordinary skill would have selected the components recited in the claimed invention out of the myriad possibilities of "vehicles." Hence, Applicant respectfully concludes that the claimed invention itself has served as a "blueprint" for the Examiner's rejection.

The courts have made it clear that the disclosure of one reference can be properly combined with the disclosure of one or more additional references *only if* the requisite motivation for the combination can be found in the reference itself. As stated by the Federal Circuit:

> In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. . . . "[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ 2d 1596, 1598 (Federal National Mortgage Association. Cir. 1988).

In re Fritch, 23 USPQ 2d 1780, 1783 (Federal National Mortgage Association. Cir. 1992). It is also well-settled that a *prima facie* case of obviousness cannot be predicated on hindsight reconstruction. As stated by the Board:

> In the instant application, the examiner has done little more than cite references to show that one or more elements or subcombinations thereof, when each is viewed in a vacuum, is known. The claimed invention, however, is clearly directed to a combination of elements. That is to say, appellant does not claim that he has invented one or more new elements but has presented claims to a new combination of elements. To support the conclusion that the claimed combination is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed combination or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references. . . . Based upon the record before us, we are convinced that the artisan would not have found it obvious to selectively pick and choose elements or concepts from the various references so as to arrive at the claimed invention without using the claims as a guide. It is to be noted that simplicity and hindsight are not proper criteria for resolving the issue of obviousness.

Ex parte Clapp, 227 USPQ 972, 973 (B.P.A.I. 1985). Similarly, the Federal Circuit has stated:

> It is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teachings of the prior art so that the claimed invention is rendered obvious. This court has previously stated that "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." (quoting *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ 2d 1596, 1600 (Federal National Mortgage Association. Cir. 1988).

In re Fritch, 23 USPQ 2d 1780, 1784 (Federal National Mortgage Association. Cir. 1992). In the present case, the Examiner admits that the '825 patent does not explicitly teach a composition comprising all of the components claimed but she merely asserts that all the claimed components are well known and commonly used in the art.[1] Because one of ordinary skill in the art would not have been motivated to use

[1] In *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987), the Examiner's rejection, which was based upon the prior art and the fact that each of the three components of the composition used in the claimed method was conventionally employed in the art for treating cooling water systems, was sustained by the Board of Appeals, which held that it would have been *prima facie* obvious to employ these components in combination for their known functions and to optimize the amount of each additive. Applicant appealed arguing that the PTO's position represented hindsight reasoning or, at

a "vehicle" for a therapeutic purpose, let alone select the particular components of the claimed invention, it would seem that the Examiner's rejection is motivated instead by hindsight reasoning. Applicant recognizes that it may sometimes be difficult to guard against the insidious effects of hindsight reasoning, but it is incumbent upon the Examiner to resist the urge to use the Applicant's own disclosure to find a motivation to combine the teachings of the state of the art.

Thus, the Examiner's rejection is apparently based on hindsight reasoning and, thus, is improper in the first instance. For this reason alone, the rejection under Section 103(a) cannot be sustained and should be withdrawn.

It is believed that the rejections have been overcome. Applicant respectfully requests that the Examiner give favorable reconsideration to the pending claims of the application. An early action indicating allowability is cordially solicited.

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best, established that it would have been "obvious to try" various combinations of known agents. The Federal Circuit agreed with the Appellant, noting that obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination. In the present case, in addition to cautioning the Examiner against hindsight reasoning, Applicant respectfully points out that the components recited in the claimed invention are conventionally employed as a "vehicle," to which no therapeutic activity is conventionally associated.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for this Response, or credit any overpayment to Deposit Account No. 50-1710.

In the event that an extension of time is required, or may be required in addition to that requested in a petition for an extension of time, the Commissioner is hereby requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-1710.

Respectfully submitted,
KATTEN MUCHIN ZAVIS ROSENMAN

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Date: December 2, 2002

APPENDIX A

ATTY. DKT. NO. 320607.00100
CUSTOMER NO. 27160

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	R. Vasquez Lipi	Examiner: Berman, A.
Serial No.:	09/810,660	
Filed:	March 19, 2001	Art Unit: 1617

For: TOPICAL MEDICAMENT FOR SKIN INJURIES AND DISORDERS

DECLARATION UNDER 37 C.F.R. §1.132

Commissioner for Patents
Washington, DC 20231
Sir:

I, Lydia Tabuke, M.D., do hereby make the following declaration:

1. I received an advanced degree in May 2002 from the Johns Hopkins Bloomberg School of Public Health, Master in Public Health with Interest in Epidemiology and Clinical Trials; in 1994 I was also awarded a Bachelors in Surgery and Bachelors in Medicine from the University of Nairobi, Medical School, Nairobi, Kenya and was the recipient in 1999 of a Fellowship in Pediatric Infectious Disease from Albany Medical College, Albany, New York;

2. I am currently employed by CAC Pharmaceuticals, Inc., the assignee of record of the above-referenced patent application; in my capacity as Manager, Research and Development, among other things, I am responsible for overseeing clinical trials worldwide, including managing all aspects of clinical trials-background research, clinical protocols, data management, finalizing of study reports and site visits; I also collaborate and participate in company deliberations involving intellectual property issues;

3. I have read and studied the specification and pending claims of the above-referenced patent application; I have also studied the outstanding office action, which was mailed July 2, 2002;

4. I understand from this office action that the Examiner has rejected the pending claims based on an allegation of obviousness over the combined disclosures of certain prior art references, which were cited by the Examiner in this office action; I also understand that as part of the process of reconsidering rejected claims, the United States Patent and Trademark office takes into consideration evidence of surprising or unexpected results; what follows is a description of the results of one *in vivo* study involving human burn patients, which in my opinion constitutes surprising or unexpected results;

5. Patients for a double-blinded randomized clinical trial were recruited from the Surgical Division of General San Martin Hospital, La Plata, Buenos Aires Province, Argentina; a total of 132 patients with superficial burns participated in the study; a topical preparation (hereinafter, the "SENCIL® preparation") falling within the scope of claim 1, as amended, and comprising beeswax, an oleaginous base consisting essentially of olive oil, sunflower oil, almond oil, cod liver oil and castor oil, and white petrolatum as excipient was used in the clinical trial;

6. Good results were observed, indicating that the SENCIL® preparation used, while not including a drug conventionally utilized to treat burns (indeed, the SENCIL® preparation used contained no drug of any kind), performed surprisingly or unexpected better than silver sulfadiazine (hereinafter, "SSD"), a drug preparation that is a standard for treatment of burns; for example, superficial burn patients took 11.3 days on average to heal versus 15.8 days on average when on SSD; moreover, pain control was also better with the SENCIL® preparation, in which 55 individuals or 88% of the burn patients on the SENCIL® preparation experienced no pain as opposed to only 50 individuals or 75% of the burn patients on SSD (I note further that effective pain relief is advantageous in modulating the acute immune response); lastly, tolerance to treatment was better with the SENCIL® preparation, with a mere 6% of patients on the SENCIL® preparation failing to tolerate the inventive preparation compared with 17% of patients on SSD failing to tolerate the standard treatment;

7. In addition, comparative studies involving the SENCIL® preparation and SSD further showed a surprising or unexpected benefit from the use of the SENCIL® preparation, namely, that minimal pain was experienced by the burn patients when changing the dressings of their wounds because the SENCIL® preparation did not cause the dressings to adhere to the wound; moreover, there was no need to clean the wound prior to the next application of the SENCIL® preparation; the gauze was easily pulled off, and minimal slough and scar tissue was encountered, leaving a clean wound and making treatment virtually painless;

8. The SENCIL® preparation caused no apparent allergies in the patients, and no contraindication to the use of the SENCIL® preparation is known; SSD is contra-indicated in patients with allergy to sulfa drugs;

9. I consider these results using the SENCIL® preparation surprising or unexpected, especially considering that the SENCIL® preparation used contained no "active" or "therapeutic" ingredient, which one of ordinary skill in the pharmaceutical arts would have considered the equivalent of a steroid or sulfa drug commonly associated with standard burn treatments.

10. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: 12/02/02.

By: JTabuke

Lydia Tabuke, M.D.

APPENDIX B

Marked Version of Claims Showing Changes Made

1. (Twice Amended) A composition for application to the skin or mucosal surface[, comprising] to treat burns and other injuries and disorders, consisting essentially of:

a) from about 10 and about 50 percent by weight of beeswax;

b) an oleaginous base including olive oil, sunflower oil, almond oil, cod liver oil[,] and castor oil [and beeswax,]; and

[b)] c) a pharmaceutically[-]acceptable excipient.

25. (Amended) A method for treating [an injury to the skin or mucosa] burns and other injuries and disorders of the skin or mucosal surface, which comprises applying to the [injured] site in need of treatment an effective amount of a composition [comprising between] consisting essentially of: a) from about 10 and about 50 percent by weight of beeswax[, a pharmaceutically-acceptable emollient]; b) an oleaginous base including olive oil, sunflower oil, almond oil, cod liver oil and castor oil; and c) a pharmaceutically[-] acceptable excipient.